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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/531,427      | 04/15/2005  | Toshiyuki Miyata     | 0020-5363PUS1       | 2681             |

2292 7590 04/18/2008  
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| EXAMINER |
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KIM, ALEXANDER D

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1656

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| NOTIFICATION DATE | DELIVERY MODE |
|-------------------|---------------|

04/18/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/531,427 | <b>Applicant(s)</b><br>MIYATA ET AL. |  |
|                              | <b>Examiner</b><br>ALEXANDER D. KIM  | <b>Art Unit</b><br>1656              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 January 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 5,6,9,11-18 and 20-24 is/are pending in the application.
- 4a) Of the above claim(s) 15-16 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5,6, and 18 is/are allowed.
- 6) ☒ Claim(s) 9,12,13,17,20, 22 and 23 is/are rejected.
- 7) ☒ Claim(s) 11,14,21 and 24 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Application Status***

1. In response to the previous Office action, a non-Final rejection (mailed on 02/23/2006), Applicants filed a response and amendment received on 06/07/2006. Said amendment cancelled Claims 1-4, 7-8 and 10; amended Claims 5-6, 9, 11-14 and 17-18; and added new Claims 20-24.

Claims 5-6, 9, 11-18 and 20-24 are pending in the instant Office action. Claims 15-16 are withdrawn as non-elected inventions.

Thus, Claims 5-6, 9, 11-14, 17-18 and 20-24 will be examined herein.

### ***Withdrawn-Compliance with Sequence Rules***

2. The previous non-compliance with the Sequence Rules is withdrawn by virtue of Applicants' argument.

### ***Withdrawn-Objections to the Specification***

3. The previous objection to the specification because the title is not descriptive of the claims is withdrawn by virtue of Applicants' amendment.

4. The previous objection to the specification for reciting "Try1605-Met1606" on page 3, line 14 is withdrawn by virtue of Applicants' amendment.

5. The previous objection to the specification because the "Brief Description of the Drawings" on page 9 discloses many amino acid sequences fused with GST without appropriate point of reference (i.e., appropriate SEQ ID NO) is withdrawn by virtue of Applicants' amendment.

***Maintained-Objections to the Specification***

6. The previous objection to the specification (page 32 line 10) for reciting an amino acid sequences fused to GST without appropriate SEQ ID NO is maintained.  
Appropriate correction is required.

***Withdrawn-Claim Objections***

7. The previous objection to the Claim for using abbreviation "ADAMTS-13" or "VWF" is withdrawn by virtue of Applicants' amendment.

***Claim Objections***

8. Claims 11-14 and 21-24 are objected to because of the following informalities:

(a) Claim 11 is objected to because Claim 11 would be more clear if the claim recites "further having a tag sequence...". Appropriate correction is required.

(b) Claims 12-14 and 21-24 are objected because they depend from the objected Claim 11,

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 5-6, 9, 11-14, 17-18 and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These rejections are necessitated by the instant amendment.

(a) Claim 5 and 6 (Claim 9, 11-14, 17-18 and 20-24 dependent therefrom) recites "a disintegrin-like and metalloprotease with thrombospondin type-1 motif, 13". It is unclear what is encompassed by the limitation of "a disintegrin-like" and "metalloprotease with thrombospondin type-1 motif". Is there two distinct structure (that is a disintegrin-like and metalloprotease with thrombospondin type-1 motif, 13) for ADAMTS-13, which having the substrate as claimed in Claim 5 and 6). Appropriate clarification is required.

(b) Claims 12, 13 and 17 (Claims 22 and 23 dependent therefrom) recite "the mutant substrate polypeptide for ADAMTS-13 according to claim 11". There is insufficient antecedent basis for this limitation in the claims. Claim 11 does not disclose any mutant substrate polypeptide and it is unclear which specific mutant substrate polypeptide for ADAMTS-13 (if any) is encompassed in Claims 12 and 13. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 9 and 20 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant rejection is necessitated by the amendment in Claim 9 changing dependency to different polypeptide as well as adding broad functions encompassed by "the specificity".

The rejection was stated in the previous office action as it applied to previous Claims 1-14 and 17-18. In response to this rejection, applicants have cancelled Claims 1-4, 7-8 and 10; amended Claims 5-6, 9, 11-14 and 17-18; and added new Claims 20-24; and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that amended claims directed to a polypeptide having sequence identity of at least 90% or higher compared to the SEQ ID NO: 4 are further limited by the added phrase "which retains the specificity to ADAMTS-13", which skilled person in the art can easily practice the inventions relation to the mutant polypeptides as claimed.

However, the instant application disclose GST fused SEQ ID NO: 4. The breadth of claim encompasses any amino acid sequence having 90% identity to SEQ ID NO: 4 (i.e., the polypeptide of Claim 5) and having the specificity for ADAMTS-13, wherein the specificity is unclear as disclosed above (see 35 USC 112, 2nd paragraph). The prior art and the instant specification do not describe any polypeptide or any variant thereof within 90% and having any specificity sufficiently to represent the correlation between the structure of polypeptide (e.g., any polypeptide having 90% identity to SEQ ID NO: 4 of Claim 5) and function of the specificity (that includes any specificity) for ADAMTS-13. Thus, the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the full scope of claimed genus by the instant specification.

11. Claims 9 and 20 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for a substrate polypeptide for an isolated polypeptide of SEQ ID NO: 4; does not reasonably provide enablement for an amino acid having 90% identity to SEQ ID NO: 4 and retains "the specificity for ADAMTS-13", wherein the specificity includes any specificity. The instant rejection is necessitated by the amendment in Claim 9 changing dependency to different polypeptide as well as adding broad functions encompassed by "the specificity".

The rejection was stated in the previous office action as it applied to previous Claims 1-14 and 17-18. In response to this rejection, applicants have cancelled Claims 1-4, 7-8 and 10; amended Claims 5-6, 9, 11-14 and 17-18; and added new Claims 20-

24; and traverse the rejection as it applies to the newly amended claims. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that instant Claims 5, 6, 9, 11-14 and 17-18 has been amended to limit the substrate polypeptide to SEQ ID NO: 4, 5, or at least 90% of the SEQ ID NO: 4, wherein the 90% is further limited by the phrase "which retains the specificity to ADAMTS-13". Applicants also argue that claimed mutant can be practiced "easily" in view of 37 CFR §1.132 Declaration filed on 1/16/2007 by one of inventors.

The declaration disclose mouse and human polypeptide, each having a polypeptide of Asp1596 and Arg1668, which have 86.3% identity to each other. The declaration also teach how to prepare two polypeptide (human and mouse) and these were cleaved by the human plasma. However, the disclosure of one example which is 86.3% polypeptide does not enable every embodiment encompassed by the instant claims that is polypeptide of 90%-100% of SEQ ID NO: 4 and must have the specificity for ADAMTS-13 as well. The nature of the invention is drawn to a substrate polypeptide for ADAMTS-13 protease, wherein the polypeptide is SEQ ID NO: 4. However, the breadth of claim includes any polypeptide having at least 90% to SEQ ID NO: 4 and retaining any specificity for ADAMTS-13, wherein the specificity is not limited to the specificity of protease action by ADAMTS-13. The instant specification teach SEQ ID NO: 4. However, applicants and prior art disclose no direction or guidance on how to make and use any other polypeptide for ADAMTS-13, wherein the polypeptide has at least 90% to SEQ ID NO: 4 and retaining any specificity for ADAMTS-13. Thus, the



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specification and prior art fail to describe how to make and use the full scope of claimed genus sufficiently. Therefore, it is unpredictable for any polypeptide encompassed by the instant claims and having any specificity for any ADAMTS-13 from any source. Thus, it is unpredictable for one skilled in the art to make and use the full scope of claimed polypeptide that is at least 90% identity to SEQ ID NO: 4 and having any specificity as described above in the breadth of claims. The said unpredictability makes the relative skill required in the art very high. For all of the above reason, it would require undue experimentation necessary for claimed substrate polypeptide having "the specificity" for any ADAMTS-13.

***Withdrawn-Claim Rejections - 35 USC § 101***

12. The previous rejection of Claims 1-10 under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter is withdrawn by virtue of Applicants' amendment.

***Withdrawn-Claim Rejections - 35 USC § 102***

13. The previous rejection of Claims 1-14 and 17-18 under 35 U.S.C. 102(b) as being anticipated by Girma et al. (1986, Blood, vol. 67, pages 1356-1366) is withdrawn by virtue of Applicants' amendment.

***Conclusion***

14. Claims 5, 6 and 18 are allowed; and Claims 9, 11-14, 17 and 20-24 are not allowed for the reasons identified in the numbered sections of this Office action.

Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/  
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./  
Primary Examiner, Art Unit 1652